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Prevalence, patterns, and causes of anemia in cancer patients: A prospective observational study

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Abstract

Background: Anemia is a common and clinically significant comorbidity in cancer patients, adversely affecting quality of life, treatment tolerance, and outcomes. The etiology of cancer-associated anemia is often multifactorial and under-evaluated in routine practice. **Aim:** To determine the prevalence, morphological patterns, etiological distribution, and predictors of anemia in cancer patients.

Methods: This prospective observational study was conducted from May to September 2025 at a tertiary care oncology center in New Delhi. Adult cancer patients were evaluated using complete blood counts, peripheral smear examination, and relevant biochemical investigations including iron profile and vitamin assays. Anemia was classified morphologically and etiologically. Multivariable logistic regression analysis was performed to identify independent predictors of anemia.

Results: Among 120 patients, anemia was present in 86 (71.7%). Moderate anemia was most common. Normocytic (44.2%) and microcytic (39.5%) patterns predominated. Functional iron deficiency was the leading etiology (33.7%), followed by anemia of chronic disease (24.4%) and absolute iron deficiency (20.9%). Advanced/metastatic disease, hematological malignancy, and chemotherapy were significant predictors of anemia.

Conclusion: Anemia is highly prevalent and multifactorial in cancer patients, warranting systematic evaluation to guide targeted supportive management.

Keywords: Cancer-associated anemia, Functional iron deficiency, Morphological classification, Chemotherapy, Supportive oncology

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Introduction:

Anemia is one of the commonest comorbidities in patients with malignancy and it may be present at diagnosis or develop/worsen during treatment, contributing to fatigue, reduced performance status, treatment delays, dose reductions, and poorer outcomes [1]. Importantly, cancer-associated anemia is usually multifactorial, with overlapping mechanisms such as chronic inflammation (hepcidin-mediated iron sequestration), blood loss, nutritional deficiency, renal dysfunction, marrow suppression from chemotherapy/radiotherapy, and marrow infiltration in selected cancers [1]. Among the etiological patterns, iron deficiency may be absolute or functional (adequate stores but restricted iron availability for erythropoiesis), and functional iron deficiency (FID) is increasingly recognized in cancer due to inflammation and treatment effects [2]. Real-world evidence shows gaps in routine evaluation for treatable causes (iron, vitamin B12, folate), supporting the need for structured prospective workup and classification by indices/peripheral smear and iron studies [3]. In low- and middle-income settings, consensus guidance also emphasizes systematic evaluation (CBC, morphology, reticulocyte count, iron profile, B12/folate) to distinguish anemia types and guide supportive care appropriately [4]. The current research planned to prospectively determine the prevalence and distribution of anemia types (microcytic, normocytic, macrocytic; iron deficiency absolute/functional; B12/folate deficiency; mixed patterns) among cancer patients prior to and during oncology care, and to identify common clinical correlates.

Methods:

This prospective observational study was conducted in the department of Pathology and Medical Oncology at Action Cancer Hospital, New Delhi, during the period May to September 2025. Consecutive adult patients with a confirmed diagnosis of malignancy (solid tumors and hematological malignancies) who attended the oncology outpatient department or were admitted for evaluation/treatment during the study period were enrolled after obtaining Institutional Ethics Committee approval. Written informed consent was obtained from each participant prior to recruitment. Patients with known hemoglobinopathies, recent major hemorrhage/trauma, pregnancy, or those who had received blood transfusion within the preceding 4 weeks were excluded to avoid misclassification of anemia type. Baseline demographic details, cancer site/type, clinical stage (as documented by the oncology team), treatment status (newly diagnosed,

on chemotherapy, on radiotherapy, or follow-up), comorbidities, and relevant drug history were recorded in a structured case record form.

All enrolled participants underwent standardized hematological evaluation at enrolment. Venous blood samples were collected under aseptic precautions and analyzed using an automated hematology analyzer for hemoglobin, hematocrit, RBC indices (MCV, MCH, MCHC, RDW), total leukocyte count, differential count, and platelet count. Peripheral blood smear examination (Leishman stain) was performed for morphological classification of anemia and to look for anisopoikilocytosis, hypochromia, macro-ovalocytes, polychromasia, nucleated RBCs, and leukoerythroblastic picture when present. Reticulocyte count was performed where clinically indicated to assess marrow response. Anemia was defined and graded based on hemoglobin thresholds used in routine oncology practice, and was categorized morphologically into microcytic, normocytic, and macrocytic patterns using MCV cut-offs, supported by smear findings. Based on the initial work-up, a directed biochemical evaluation was performed to identify the etiology of anemia.

Iron status was assessed using serum ferritin, serum iron, total iron binding capacity (TIBC), and transferrin saturation (TSAT), and anemia was further classified as absolute iron deficiency (low ferritin with low TSAT), FID (normal/high ferritin with low TSAT), anemia of inflammation/chronic disease pattern, vitamin B12 deficiency, folate deficiency, mixed etiology, and other causes as applicable. Serum vitamin B12 and serum folate were estimated in patients with macrocytosis, dimorphic blood picture, unexplained anemia, or clinical suspicion of nutritional deficiency. Serum creatinine and estimated glomerular filtration rate were documented to evaluate anemia related to renal dysfunction, and liver function tests were reviewed when clinically relevant. Where bone marrow involvement was suspected clinically or on peripheral smear (unexplained pancytopenia, leukoerythroblastic smear, circulating blasts), bone marrow aspiration/biopsy findings, if performed as part of routine care, were recorded. All laboratory procedures were carried out in the hospital central laboratory following internal quality control protocols, and data were entered contemporaneously to minimize missing values and ensure uniform classification across participants.

Statistical analysis: Data were entered into Microsoft Excel and analyzed using SPSS version 22. Continuous variables were expressed as mean ± SD or median (IQR) based on data distribution, while categorical variables were summarized as frequency and percentage. Normality was assessed using the Shapiro–Wilk test. Group comparisons were performed using the independent t-test or Mann–Whitney U test for two groups and ANOVA or Kruskal–Wallis test for more than two groups. Associations between categorical variables were analyzed using the Chi-square or Fisher's exact test. Correlation analyses were done using Pearson or Spearman methods. Binary logistic regression identified independent predictors of anemia, and results were expressed as odds ratios with 95% confidence intervals. A p value <0.05 was considered statistically significant.

Results:

Out of the 120 cancer patients enrolled, anemia was observed in 86 patients, resulting in an overall prevalence of 71.7% (Table 2). The mean hemoglobin level among anemic patients was 9.4 ± 1.6 g/dL, with moderate anemia being the most common severity (47.7%), followed by mild (32.6%) and severe anemia (19.7%). Anemia was more frequently noted in patients with advanced or metastatic disease and in those receiving chemotherapy compared to newly diagnosed patients (Table 1). Morphological evaluation demonstrated normocytic anemia as the predominant pattern (44.2%), followed closely by microcytic anemia (39.5%), while macrocytic and dimorphic patterns together constituted 16.3% of cases (Table 3). Peripheral smear findings corroborated automated hematological parameters and were useful in identifying mixed etiologies and marrow stress in selected cases. Etiological analysis revealed FID as the leading cause of anemia (33.7%), followed by anemia of chronic disease (24.4%) and absolute iron deficiency (20.9%). Nutritional deficiencies due to vitamin B12 and/or folate were identified in 11.6% of patients, predominantly among those with macrocytic or dimorphic anemia, while mixed etiologies were observed in 9.4% (Table 4). Multivariable logistic regression analysis identified advanced disease stage, hematological malignancy, and ongoing chemotherapy as significant predictors of anemia, as illustrated in the forest plot (Figure 1). Overall, these findings highlight the high burden and multifactorial nature of anemia in oncology patients and underscore the importance of systematic morphological and biochemical evaluation to guide optimal supportive care.

Discussion:

Table 1 shows that the study cohort predominantly comprised middle-aged to older adults (mean age 56.4 ± 11.8 years) with a male preponderance, reflecting the typical age distribution of many common solid malignancies presenting to tertiary oncology services. A large proportion of patients had solid tumors (80%) and nearly two-thirds had advanced/metastatic disease (61.7%), indicating that many patients were evaluated at a relatively late stage, where systemic inflammation, nutritional

compromise, and disease burden can contribute to cytopenias and poorer baseline reserves [3]. About half of the cohort was receiving chemotherapy (51.7%), which is clinically relevant because cytotoxic therapy is a well-recognized driver of anemia through marrow suppression and impaired erythropoiesis, often superimposed on pre-existing cancer-related anemia [5]. The presence of hematological malignancies (20%) is also important when interpreting baseline characteristics, as these cancers more frequently involve marrow infiltration and dysregulated hematopoiesis, resulting in a higher anemia burden compared with many untreated solid tumors [3]. Overall, the baseline profile in Table 1 supports the rationale for systematic etiological evaluation of anemia in routine oncology practice, particularly in advanced disease and during active treatment, where functional iron restriction and other multifactorial mechanisms commonly coexist and may be clinically correctable [2].

Table 2 highlights a high prevalence of anemia (71.7%) among the studied cancer patients, underscoring anemia as a major and persistent comorbidity in oncology practice. This prevalence is consistent with earlier prospective and real-world studies reporting anemia in 60–80% of patients with malignancy, particularly in those with advanced disease and during active treatment [6]. The mean hemoglobin level of 9.4 ± 1.6 g/dL indicates that most patients had clinically significant anemia rather than incidental laboratory abnormalities, which has direct implications for quality of life, functional capacity, and tolerance to anticancer therapy [5]. Moderate anemia was the most common category (47.7%), followed by mild anemia, while nearly one-fifth of patients had severe anemia, a finding of concern as severe anemia is associated with increased transfusion requirements, treatment interruptions, and poorer outcomes [5]. The observed distribution of anemia severity reflects the cumulative effects of chronic inflammation, nutritional deficiencies, marrow suppression, and disease burden that typically evolve over the course of cancer progression and treatment [1]. These findings reinforce the need for routine screening and grading of anemia in cancer patients, as recommended by international supportive care guidelines, to enable early identification and timely intervention. Overall, the data presented in Table 2 emphasize that anemia in cancer is not only highly prevalent but also frequently moderate to severe, warranting systematic evaluation and proactive management to optimize supportive care and treatment continuity.

Table 3 presents the morphological patterns of anemia among anemic cancer patients and demonstrates that normocytic anemia (44.2%) was the most common type, followed closely by microcytic anemia (39.5%), while macrocytic and dimorphic patterns together accounted for a smaller proportion. The predominance of normocytic anemia is well documented in malignancy and is typically attributed to anemia of chronic disease and inflammation, where cytokine-mediated suppression of erythropoiesis and altered iron metabolism result in reduced hemoglobin levels without significant changes in red cell indices [7]. This pattern is especially common in patients with advanced disease and ongoing chemotherapy, as seen in the present cohort. Microcytic anemia constituted a substantial proportion of cases, reflecting the high burden of iron deficiency both absolute and functional in cancer patients. Chronic blood loss, poor nutritional intake, and inflammation-induced iron sequestration are important contributors to this pattern, particularly in gastrointestinal and gynecological malignancies [2]. Peripheral smear examination played a crucial complementary role by confirming hypochromia, anisopoikilocytosis, and dimorphic pictures, thereby improving etiological classification beyond automated indices alone. Macrocytic and dimorphic anemia, although less frequent, are clinically significant as they often point toward nutritional deficiencies (vitamin B12 or folate), chemotherapy-related marrow toxicity, or mixed etiologies. Early identification of these patterns is important, as targeted correction can improve hemoglobin levels and treatment tolerance [1]. Overall, the findings in Table 3 highlight the heterogeneity of anemia in cancer patients and reinforce the importance of integrating red cell indices with peripheral smear morphology to guide focused biochemical evaluation and appropriate supportive management.

Table 4 depicts the etiological spectrum of anemia in the cohort and demonstrates that FID was the leading cause (33.7%), followed by anemia of chronic disease/inflammation (24.4%) and absolute iron deficiency (20.9%), confirming that iron-restricted erythropoiesis is central to cancer-associated anemia [2]. FID is particularly relevant in malignancy because inflammatory cytokines upregulate hepcidin, reducing intestinal iron absorption and trapping iron in macrophages, which produces low transferrin saturation despite normal or raised ferritin and contributes to poor response to oral iron therapy [2]. The notable proportion of anemia of chronic disease (24.4%) further supports an inflammation-driven pathophysiology, especially in advanced cancers and during systemic therapy, where marrow suppression and reduced erythropoietin responsiveness may coexist [4]. Absolute iron deficiency (20.9%) in Table 4 likely reflects chronic occult blood loss (especially gastrointestinal tumors), poor dietary intake, and increased iron demand, and it is clinically important because it is potentially correctable and may reduce transfusion need when diagnosed early [4]. Nutritional

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deficiencies due to vitamin B12 and/or folate accounted for 11.6%, aligning with the macrocytic/dimorphic patterns seen on morphology, and emphasizing the need for routine assessment in patients with inadequate intake, malabsorption, or prolonged treatment-related anorexia [4]. Mixed etiologies (9.4%) highlight that cancer anemia is frequently multifactorial, and a single "one-test" approach may miss overlapping causes [1]. Overall, Table 4 supports a structured workup combining morphology with iron indices and vitamin assays to enable targeted interventions (iron therapy, nutritional correction, and supportive strategies) and to optimize treatment continuity.

Figure 1 illustrates the independent predictors of anemia in cancer patients after adjustment for relevant confounders and clearly demonstrates that advanced or metastatic disease**,** hematological malignancy, and ongoing chemotherapy were significantly associated with higher odds of anemia, as their confidence intervals did not cross the null value (OR = 1) [1]. This finding is biologically plausible, as advanced disease is associated with heightened inflammatory burden and marrow suppression, while hematological malignancies directly impair erythropoiesis through marrow infiltration and dysregulated hematopoietic pathways [7]. Chemotherapy-related anemia, highlighted in Figure 1, reflects cumulative myelotoxic effects, reduced erythropoietin response, and treatment-induced nutritional compromise, which have been consistently reported in oncology cohorts [5]. The forest plot format allows rapid comparison of effect sizes and precision across predictors, facilitating clearer clinical interpretation and identification of high-risk subgroups who may benefit from early anemia evaluation and targeted supportive interventions [4]. By integrating multiple predictors into a single visual summary, Figure 1 strengthens the overall findings of the study and supports a risk-stratified approach to anemia management in cancer patients, aligning with current supportive care recommendations that emphasize individualized assessment rather than reliance on hemoglobin values alone.

Conclusion: This prospective study demonstrated a high prevalence of anemia among cancer patients, with the majority exhibiting moderate severity and multifactorial etiology. Normocytic and microcytic patterns were predominant, while functional iron deficiency emerged as the leading cause, underscoring the role of inflammation-mediated iron dysregulation in malignancy. Advanced disease stage, hematological malignancies, and ongoing chemotherapy were identified as significant independent predictors of anemia. These findings emphasize the need for routine, structured morphological and biochemical evaluation of anemia in oncology practice to enable early identification of treatable causes and to optimize supportive care, treatment tolerance, and overall patient outcomes.

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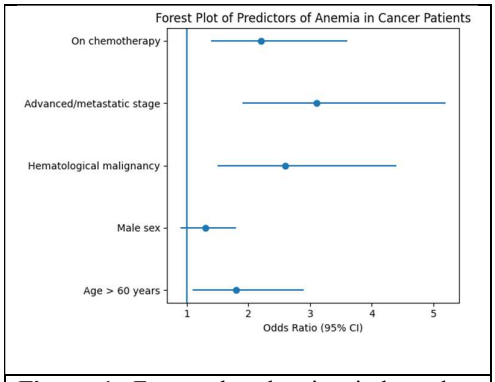

Figure 1: Forest plot showing independent predictors of anemia in cancer patients

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Table 1: Baseline demographic and clinical characteristics (n = 120)	
Variable	**Number (%)**
Age (years), mean ± SD	56.4 ± 11.8
Male	68 (56.7)
Solid malignancies	96 (80.0)
Hematological malignancies	24 (20.0)
Advanced/metastatic disease	74 (61.7)
Newly diagnosed (pre-treatment)	58 (48.3)
On chemotherapy	62 (51.7)

Table 2: Prevalence and severity of anemia among the study members	
Parameter	**Number (%)**
Anemia present	86 (71.7)
Mild anemia	28 (32.6)
Moderate anemia	41 (47.7)
Severe anemia	17 (19.7)
Mean hemoglobin (g/dL)	9.4 ± 1.6

Table 3: Morphological classification of anemia (n = 86)	
Type of anemia	**Number (%)**
Microcytic	34 (39.5)
Normocytic	38 (44.2)
Macrocytic	9 (10.5)
Dimorphic	5 (5.8)

Table 4: Etiological distribution of anemia among the study members	
Etiology	**Number (%)**
Functional iron deficiency	29 (33.7)
Absolute iron deficiency	18 (20.9)
Anemia of chronic disease	21 (24.4)
Vitamin B12 / folate deficiency	10 (11.6)
Mixed etiology	8 (9.4)